Are orthodontic systematic reviews registered a priori in PROSPERO?

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Abstract: INTRODUCTION: Aim of this study was to assess the registration of orthodontic systematic reviews in PROSPERO. METHOD: Seven databases were searched for orthodontic systematic reviews published in 2012-2016. After duplicate study selection and data extraction, descriptive statistics, followed by chi-square/Fisher exact tests were calculated. Finally, bivariable/multivariable regression with relative risks (RR) and 95% confidence intervals (CIs) was used. RESULTS: A total of 182 orthodontic systematic reviews were identified, 37 (20.3%) of which were registered in PROSPERO, with registration rates ranging from 4.3% in 2012 to 37.0% in 2016. Differences in review registration were found according to publication year, geographic origin, multicentre status, funding, and journal category. After controlling for confounders, each additional year was associated with increased registration probability (RR = 1.51; 95% CI = 1.19-1.93). Reviews from South America were more likely to be registered than reviews from Europe (RR = 1.49; 95% CI = 1.06-2.11). Finally, reviews published in orthodontic specialty journals were more likely to be registered than reviews in general dentistry journals (RR = 1.87; 95% CI = 1.02-3.49). CONCLUSIONS: A small percentage of orthodontic systematic reviews was registered a priori, although improvement signs have been seen since the initiation of PROSPERO.

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Title Page

Are orthodontic systematic reviews registered *a priori* in PROSPERO?

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Short title: Registration of orthodontic systematic reviews

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ABSTRACT

Introduction: *A priori* registration of systematic review protocols in PROSPERO can help restrict the risk of biased *post hoc* decisions in review procedures, such as selective outcome reporting. Aim of this study was to assess the registration of orthodontic systematic reviews in PROSPERO and examine predictive factors of systematic review registration.

Method: Seven databases were searched for systematic reviews with/without meta-analysis in orthodontics published between 2012-2016. After duplicate study selection and data extraction, descriptive statistics, followed by chi-square/Fisher exact tests were calculated. Finally, factors associated with systematic review registration were investigated by bivariable/multivariable regression models with Relative Risks (RR) and the corresponding 95% Confidence Intervals (CIs).

Results: A total of 182 orthodontic systematic reviews were identified, 37 (20.3%) of which were registered in PROSPERO, with registration rates ranging from 4.3% in 2012 to 37.0% in 2016. Crude differences in systematic review registration rates were found according to publication year, geographic origin, inclusion of multiple centers, funding, and journal category. After controlling for confounders, a 51% increase in registration probability for each year was seen (RR=1.51; 95% CI=1.19-1.93). Additionally, systematic reviews from South America were 49% more likely to be registered in PROSPERO than single-center systematic reviews (RR=1.49; 95% CI=1.06-2.11). Finally, orthodontic systematic reviews published in specialty journals were 87% more likely to be registered than systematic reviews in general dentistry journals (RR=1.87; 95% CI=1.02-3.49).

Conclusions: A small percentage of orthodontic systematic reviews was registered *a priori*, although improvement signs have been seen since the initiation of PROSPERO. However, it is important to note that sole registration in PROSPERO is not necessarily associated with robust systematic review methodology.

Introduction

Systematic reviews constitute an efficient means of synthesising the totality of evidence pertaining to a specific research question and can therefore form the ideal basis to build clinical recommendations (Patsopoulos et al. 2005), which makes them fundamental in guiding clinical medicine and future research. The main strengths of the systematic review design include the identification of all studies relevant to the research question and the use of pre-defined, reproducible, and robust methods for the phases of the systematic review in a transparent matter. However, several types of bias have been documented in various phases of the research procedure (Chavalarias and Ioannidis, 2010).

Outcome reporting bias is a form of bias occurring, when the choice of outcome reporting is influenced by the outcomes' results, with the scale usually leaning towards studies with statistically significant or 'attractive' results. Outcome reporting bias might exist in clinical trials with multiple measured outcomes, especially if these have not been transparently pre-specified in the trial's protocol (Chan et al. 2004). Likewise, a comparison between *a priori* protocols of systematic reviews and the subsequent published articles found considerable discrepancies between them, which increased the likelihood of reporting statistically significant outcomes (Kirkham et al. 2010). Therefore, this was interpreted as signs of outcome reporting bias in systematic reviews.

Registration of systematic review protocols enables the reader to check for any outcome reporting bias by comparing the outcomes between the protocol and final published article (Mathieu et al. 2009). Furthermore, a large number of systematic reviews see to have overlap in terms of eligible interventions, settings, and types of studies (Siontis et al. 2013)—something that is deemed unnecessary duplication or research waste and can be prevented by registration of the systematic review protocol (Booth et al. 2012, Moher 2013, Moher et al. 2014). The idea of protocol registration was first disseminated as the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement in 2009 (Liberati et al. 2009). Following the publication of this statement, the United Kingdom Centre for Reviews and Dissemination developed the international

prospective register of systematic reviews (PROSPERO) in 2011. PROSPERO enables the registration of any systematic review with a clinically relevant scope (provided the protocol is submitted prior to initiation of the review procedures), while providing open access to all protocols and tracking of all protocol changes. The aim of this registry and statement was to minimize reporting bias through transparency in the review process and to reduce unplanned duplication of reviews (Booth et al. 2012).

As far as we know, no study has assessed the proportion of systematic reviews having been registered in PROSPERO overall or any changes in protocol registration through time. The only exception is the recent study of Tsugimoto et al. (2017) that assessed the PROSPERO registration rate of systematic reviews published in high-impact medical journals and indicated that only 21% of them had their protocols registered. However, no data specific to the field of orthodontics was provided, while the inclusion of only high-impact journals might provide an overly optimistic image of protocol registration, due to considerable differences of systematic review quality according to journal characteristics (Papageorgiou et al. 2011, Papageorgiou et al. 2014). To this end, aim of the current study was to investigate to which extent systematic reviews in orthodontics are registered *a priori* in PROSPERO and which factors are associated with the systematic review registration.

Materials and methods

Electronic search strategies were developed and executed on January 2017 to identify systematic reviews relevant to orthodontics from MEDLINE (via PubMed), Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effects, Embase, Scopus, Web of Science, and Virtual Health Library (including LILACS and Bibliografia Brasileira de Odontologia) without restrictions for publication language or publication status (Appendix 1). As the PROSPERO register was launched in February 2011, we allowed one year for dissemination of the register and included systematic reviews from 2012 and on. Eligible for this study were orthodontic systematic

reviews with or without meta-analysis. We defined as systematic review any publication that termed itself as such and used a systematic approach to identify, select, and appraise studies in order to answer a research question. We included systematic reviews pertinent to any diagnostic-related or treatment-related aspect of orthodontics (including interdisciplinary orthodontics) in patients of any age, but we excluded subjects not directly related to orthodontics (like systematic reviews pertinent to dental / craniofacial growth, pure surgical treatment, or methodological aspects of orthodontic research). As Cochrane Reviews are consistently registered during the protocol stage, they were excluded from the present study. All other studies like narrative reviews, clinical, or *in vitro* studies were excluded. Identified reports were screened sequentially by title, abstract, and full text to check for eligibility. Additional material included as online appendix in the original articles was acquired, when needed.

Data to be collected were defined *a priori* from pilot searching of the literature and discussion among the authors, based on previous reports (Papageorgiou et al., 2011; Papageorgiou et al., 2014). Epidemiological characteristics were based on the corresponding author of each article including country, continent, and clinical setting (i.e. university or another setting). Additionally, data were extracted on publication year, number of authors, involvement of a statistician/epidemiologist, inclusion of multiple centers, funding, publication journal, and on whether the systematic review was registered in PROSPERO.

All study procedures were conducted by two authors (SS, SNP) with any disagreements resolved by a third author (TE). The two scoring authors (SS, SNP) were calibrated prior to the actual procedures in three sets of 50 papers at a time, until over 90% agreement was seen. Finally, a random set of 50 papers was checked afterwards for consistency from both authors.

For the statistical analysis, initially descriptive statistics were calculated as absolute and relative frequencies for binary outcomes. Crude differences in registration rates according to review characteristics were investigated with chi-square/ Fisher exact tests, as appropriate. Furthermore, generalized linear models for the binary family were used to evaluate the association

between registration in PROSPERO and specific systematic review characteristics. Results were expressed as Relative Risks (RR) and the corresponding 95% Confidence Intervals (CI). First, bivariable models were constructed for each characteristic. Afterwards, all characteristics with P<0.2 in the bivariable model (Maldonado and Greenland 1993), we entered in a multivariable model to identify predictors after adjusting for confounding. All analyses were performed in Stata version 14 (StataCorp LP, College Station, TX) with a two-tailed P<0.05 considered as significant.

Results

The electronic search yielded initially a total of 2 141 citations, from which 1 176 citations remained for screening after de-duplication (Figure 1; Appendix 2). After applying the eligibility criteria, a total of 182 systematic reviews were finally included, which were published between 2012 and 2016 (Table 1).

The included systematic reviews originated from at least four different continents (Table 1) and 34 different countries (Appendix 3), with the most prolific countries being Brazil (n=27; 14.8%), China (n=24; 13.2%), Italy (n=18; 9.9%), and United Kingdom (n=12; 6.6%). The most prolific continent was Europe (n=79; 43.4%) and Asia (n=50; 27.5%). From these 182 systematic reviews, the majority had a university affiliation (n=170; 93.4%), included four to six authors (n=103; 56.6%), and included more than one research centers (n=101; 55.5%). On the other hand, only few systematic reviews included a statistician/epidemiologist (n=26; 14.3%) or received funding (n=41; 22.5%). The included systematic reviews were mostly published in orthodontic specialty journals (n=94; 51.7%), followed by general dentistry journals (n=58; 31.9%), and non-dental journals (n=30; 16.5%). Finally, the identified systematic reviews included between 0 and 377 primary studies (median of 12 studies; interquartile range of 7 to 24 studies).

Out of the 182 identified systematic reviews, only 37 systematic reviews (20.3%) were registered in PROSPERO overall (Table 1). In the five years covered in this investigation, there was an increase both in the number of systematic reviews published each year and in the

percentage of published systematic reviews registered in PROSPERO, with the latter ranging from 4.3% in 2012 to 37.0% in 2016 (P<0.05; Figure 2). Significant differences in systematic review registration were found according to the country of origin, with the countries mostly contributing with registered systematic reviews being the United Kingdom (58%), followed by Brazil or Italy (both 33.3%), and the Netherlands (30.0%) (P=0.001). On a continent level, systematic reviews originating from South America were more compliant with *a priori* registration (31.0%), followed by Europe (26.6%), Asia (12.0%), North America (5.3%), and other continents (0%) (P<0.05).

The result of the bivariable and muiltivariable investigation for predictors of systematic review registration can be seen in Table 2. The bivariable analysis indicated publication year, geographic origin, multicenter status, funding, citation of the PRISMA guidelines in any part of the review's methods, and journal type as possible predictors of systematic review registration. Based on the results of the multivariable analysis, a 51% increase per year in the percentage of registered systematic reviews was seen (RR=1.51; 95% CI=1.19 to 1.93). Additionally, systematic reviews from South America were 49% more likely to be registered in PROSPERO than systematic reviews from Europe (RR=1.49; 95% CI=1.06 to 2.11). Finally, systematic reviews published in orthodontic specialty journals were 87% more likely to be registered in PROSPERO than systematic reviews published in general dentistry journals (RR=1.87; 95% CI=1.00 to 3.49).

Discussion

The present study assesses the proportion of protocol registrations in PROSPERO among systematic reviews published in orthodontic literature from 2012. The results suggest that although the proportion of systematic review registered in PROSPERO has increased in the last years from 4.3% in 2012 to 37.0% in 2016, most systematic reviews in orthodontics are still not being registered *a priori*. Factors associated with registratiojn in PROSPERO were the year of publication, the systematic review's geographical origin, and the publication journal. To our

knowledge, this is the first study to investigate how many systematic reviews in orthodontics have been registered *a priori* in PROSPERO.

The only direct comparison that can be made is with the study of Tsugimoto et al. [2017] that assessed the registration status of 284 systematic reviews published in high-impact medical journals. As can be seen in Appendix 4 for the years with overlap between the two studies (2012-2015), systematic review registration in PROSPERO was consistently lower in orthodontics than general medicine both in 2012 (4.3% versus 20.3%, respectively) and in 2015 (15.3% versus 27.3%). Differences between the two studies can be explained by differences in knowledge of epidemiology, statistics, and evidence-based study design between the fields of orthodontics and general medicine (Polychronopoulou et al. 2011). Alternatively, these differences could be explained by the fact that the study of Tsugimoto et al. [2017] was limited to high-impact medical journals, which might maintain stricter peer review procedures and might be of higher methodological quality (Fleming et al., 2014). In any case, registration of systematic reviews in orthodontics was generally limited, which can have serious implications in the transparency of evidence synthesis procedures.

A definite improvement in the registration of systematic reviews in orthodontic was seen through the period of 2012-2016, with an increase from 4.3% to 37.0%, respectively. Comparing the overlapping time period of 2012-2015 between the present study and the study of Tsugimoto et al. (2017), the increase in registered systematic reviews through time was +11.5% and +7.0% for orthodontics and medicine, respectively, indicating that a quicker improvement pace of the former. This agrees with previous studies that documented this rapid increase in systematic review production and quality (Papageorgiou et al. 2011; Papageorgiou et al. 2014; Kanavakis et al. 2016). This might be due to the quick dissemination of guidelines to improve the quality and transparency of reporting oral health research (Sarkis-Onofre et al. 2015) and the implementation of stricter peer review procedures for systematic reviews from journals.

Additionally, this increase in the production of systematic reviews in orthodontics was influenced quantitatively and quantitative by the geographic differences. At country level, great variation in registration rates was seen, with the United Kingdom having the highest registration rate that was almost twice that of the country with the next highest registration rate (58.3% to 33.3%). A possible explanation for this might be that some funding agencies supporting systematic reviews might mandate that the review protocols are registered *a priori* in PROSPERO. Registration is for example required for reviews funded by the United Kingdom's National Institute for Health Research or suggested for reviews funded by the Canadian Institutes of Health Research (Stewart et al. 2012). As can be seen by the cross-tabulation of publication year with continent of origin in Appendix 5, a clear increase in the number of produced systematic reviews per year was seen mainly for Europe, South America, and Asia. However, when looking at the % of systematic reviews registered in PROSPERO, Europe and South America showed a steady increase through time. Interestingly, systematic reviews originating from South America had 49% higher probability of being registered in PROSPERO compared to reviews originating from Europe (Table 2). This could be explained by higher methodological quality of reviews originating from South America, as has been previously reported (Fleming et al. 2013).

Interestingly, the likelikood of registration in PROSPERO was significantly higher for systematic reviews published in orthodontic specialty journals than for those published in general dentistry journals (Table 2). This might be due to the fact that unregistered systematic reviews might not get that easily accepted for publication in the more relevant to the subject orthodontic specialty journals and end up being subsequently submitted in other non-orthodontic journals.

A priori registration of systematic reviews is crucial to their transparency, since it minimizes the risk of outcome reporting bias and of the results' manipulation, by enabling comparisons between outcomes pre-defined at protocol and those included in the published paper (Mathieu et al. 2009). Furthermore, *a priori* registration helps avoid considerable waste of research resources (Ioannidis et al. 2014; Ioannidis 2016) due to overlap between multiple systematic reviews being

produced on the same subject. This is something that might happen more often than one might expect, as the authors have found out personally on three separate occasions. However, it is important to note, that the task of checking for already ongoing reviews with subject overlap lies with the review authors that aim to submit a protocol to PROSPERO and the PROSPERO staff doesn't actually check for overlaps among reviews. We believe that the task of pilot checking the existing literature on the subject prior to working on the review protocol (including the search for any ongoing reviews with overlap) lies within the tasks of all prospective authors of systematic reviews that respect the research resources they manage. Finally, the preparation and submission of a systematic review protocol might indirectly affect the methodological robustness of the systematic review, since authors need to plan and delineate in their submitted protocol every step of the review procedure from formulation of the research question, through description of the experimental and control groups, measured settings/outcomes, literature search, study selection, data extraction, risk of bias assessment, and ending with data synthesis. However, it is important to note that although PROSPERO checks all submitted protocols for relative relevance, these checks do not constitute peer review or imply approval of your systematic review methods. Therefore, this does not mean that the submitted systematic review protocols submitted in PROSPERO (or the actual review methods) are peer reviewed at this stage, and methodological issues might still exist.

As far as we know, this study is the first of its kind in the field of orthodontics and provides useful insight to the registration status of orthodontic systematic reviews published in the last five years. However, certain limitations are also present. First, as stated above, registration of a systematic review protocol is a prerequisite according to current guidelines (Liberati et al. 2009, Higgins and Green 2011), but might not necessarily mean that the review is free of methodological issues or has low risk of bias. This would need an additional assessment of either methodological quality with the AMSTAR tool (Shea et al. 2009) or of the review's risk of bias with the ROBIS tool (Whiting et al. 2016). Additionally, the results of this study are not applicable to Cochrane reviews,

which were excluded from this study, as their protocols are consistently registered beforehand. Also, the present study assessed only the registration of systematic review protocols in the PROSPERO database, since it has been the most comprehensive attempt to register review protocols, has been widely disseminated, and provides easy and open access to all review protocols. This seems that reviews with protocols registered in any other repositories were not assessed in the present study. Finally, we extracted the registration status of each systematic review on pertinent statements from within the systematic review published papers and therefore, if a registered systematic review didn't report its registration in the published paper, this was categorized as non-registered.

Conclusions

A priori registration in PROSPERO of non-Cochrane systematic review protocols in orthodontics was found to be deficient. The proportion of registered systematic reviews increased during the last five years and systematic reviews published in orthodontic specialty journals were more likely to be registered than reviews published in general dentistry journals. However, the majority of systematic reviews in orthodontics remain unregistered, which has serious implications for the transparency of the conduct of reviews, the potential reliability of their conclusions, and subsequent clinical recommendations.

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Table 1. Demographics of included sample of systematic reviews and tabulation according to registration in PROSPERO status.

					Registered		
					No	**Yes**	
Factor	**Category**	**N**	**%[$]**		**n (%[£])**	**n (%[£])**	**P[†]**
	Total	182	100.0%		145	37	
Year	2012	23	12.6%		22 (95.7%)	1 (4.3%)	0.004
	2013	24	13.2%		19 (79.2%)	5 (20.8%)	
	2014	43	23.6%		38 (88.4%)	5 (11.6%)	
	2015	38	20.9%		32 (84.2%)	6 (15.8%)	
	2016	54	29.7%		34 (63.0%)	20 (37.0%)	
Country (coded)*	Brazil	27	14.8%		18 (66.7%)	9 (33.3%)	0.001
	Canada	11	6.0%		10 (90.9%)	1 (9.1%)	
	China	24	13.2%		22 (91.7%)	2 (8.3%)	
	Greece	10	5.5%		10 (100.0%)	0 (0%)	
	Italy	18	9.9%		12 (66.7%)	6 (33.3%)	
	Netherlands	10	5.5%		7 (70.0%)	3 (30.0%)	
	United Kingdom	12	6.6%		5 (41.7%)	7 (58.3%)	
	Other	70	38.5%		61 (87.1%)	9 (12.9%)	
Continent	Europe	79	43.4%		58 (73.4%)	21 (26.6%)	0.04
	North America	19	10.4%		18 (94.7%)	1 (5.3%)	
	South America	29	15.9%		20 (69.0%)	9 (31.0%)	
	Asia	50	27.5%		44 (88.0%)	6 (12.0%)	
	Other	5	2.8%		5 (100.0%)	0 (0%)	
Affiliation	University	170	93.4%		135 (79.4%)	35 (20.6%)	1.00
	Other	12	6.6%		10 (83.3%)	2 (16.7%)	
Number of authors	1-3	53	29.1%		44 (83.0%)	9 (17.0%)	0.59
	4-6	103	56.6%		82 (79.6%)	21 (20.4%)	
	>6	26	14.3%		19 (73.1%)	7 (26.9%)	
Statistician/ epidemiologist involved	No	156	85.7%		125 (80.1%)	31 (19.9%)	0.71
	Yes	26	14.3%		20 (76.9%)	6 (23.1%)	
Multicenter	No	81	44.5%		69 (85.2%)	12 (14.8%)	0.10
	Yes	101	55.5%		76 (75.3%)	25 (24.8%)	

Funding received	No	141	77.5%		108 (76.6%)	33 (23.4%)	0.08
	Yes	41	22.5%		37 (90.2%)	4 (9.8%)	
Citation of PRISMA	No	79	43.4%		71 (89.9%)	8 (10.1%)	0.003
	Yes	103	56.6%		74 (71.8%)	29 (28.2%	
Journal type	Dental; orthodontic	94	51.7%		69 (73.4%)	25 (26.6%)	0.08
	Dental; non-orthodontic	58	31.9%		51 (87.9%)	7 (12.1%)	
	Non-dental	30	16.5%		25 (83.3%)	5 (16.7%)	
Orthodontic journal	Am J Orthod Dentofacial Orthop	21	11.5%		14 (66.7%)	7 (33.3%)	0.40
	Angle Orthod	17	9.3%		12 (70.6%)	5 (29.4%)	
	Dental Press J Orthod	5	2.7%		5 (100.0%)	0 (0%)	
	Eur J Orthod	23	12.6%		14 (60.9%)	9 (39.1%)	
	Int Orthod	1	0.5%		1 (100.0%)	0 (0%)	
	J Orofac Orthop	2	1.1%		2 (100.0%)	0 (0%)	
	J World Fed Orthod	2	1.1%		2 (100.0%)	0 (0%)	
	Korean J Orthod	1	0.5%		1 (100.0%)	0 (0%)	
	Orthod Craniofac Res	10	5.5%		10 (100.0%)	0 (0%)	
	Orthod Wav	2	1.1%		1 (50.0%)	1 (50.0%)	
	Progr Orthod	9	4.9%		6 (66.7%)	3 (33.3%)	
	Semin Orthod	1	0.5%		1 (100.0%)	0 (0%)	

*for a full list of countries of origin, see Appendix 3.
†P value from chi-square test (or from Fisher exact if >20% of cells have expected frequency less than 5 or if at least one cell is null)
[$]Percentage of systematic reviews in each factor category.
[£]Percentage of registered/non-registered systematic reviews within each factor category.

Table 2. Regression of factors associated with systematic review registration in PROSPERO.

		Univariable				Multivariable		
Factor	**Category**	**RR**	**95% CI**	**P**		**RR**	**95% CI**	**P**
Publication year	per year	1.51	1.17,1.95	0.002		1.51	1.19,1.93	0.001
Continent	Europe	Referent				Referent		
	North America	0.20	0.03,1.38	0.102		0.26	0.04,1.57	0.141
	South America	1.17	0.61,2.25	0.643		1.49	1.06,2.11	0.023
	Asia	0.45	0.20,1.04	0.062		0.56	0.24,1.28	0.167
	Other	NA						
Affiliation	University	Referent						
	Other	0.81	0.22,2.97	0.750		NT		
Authors	1-3	Ref						
	4-6	1.20	0.59,2.44	0.612		NT		
	>6	1.59	0.66,3.78	0.299		NT		
Statistician/ epidemiologist involved	No	Referent						
	Yes	1.16	0.54,2.51	0.703		NT		
Multicenter	No	Referent				Ref		
	Yes	1.67	0.90,3.12	0.106		1.59	0.93,2.72	0.088
Funding received	No	Referent				Ref		
	Yes	0.42	0.16,1.11	0.079		0.54	0.20,1.46	0.224
Citation of PRISMA	No	Referent				Ref		
	Yes	2.78	1.35,5.74	0.006		1.58	0.75,3.36	0.231
Journal type	Dental; non-orthodontic	Referent				Ref		
	Dental; orthodontic	2.20	1.02,4.77	0.045		1.87	1.00,3.49	0.049
	Biomedical	1.38	0.48,3.98	0.550		1.73	0.93,3.22	0.085

RR, relative risk; CI, confidence interval; NT, not tested.

Figure Legends

Figure 1. Flowdiagram for the identification/selection of eligible studies.

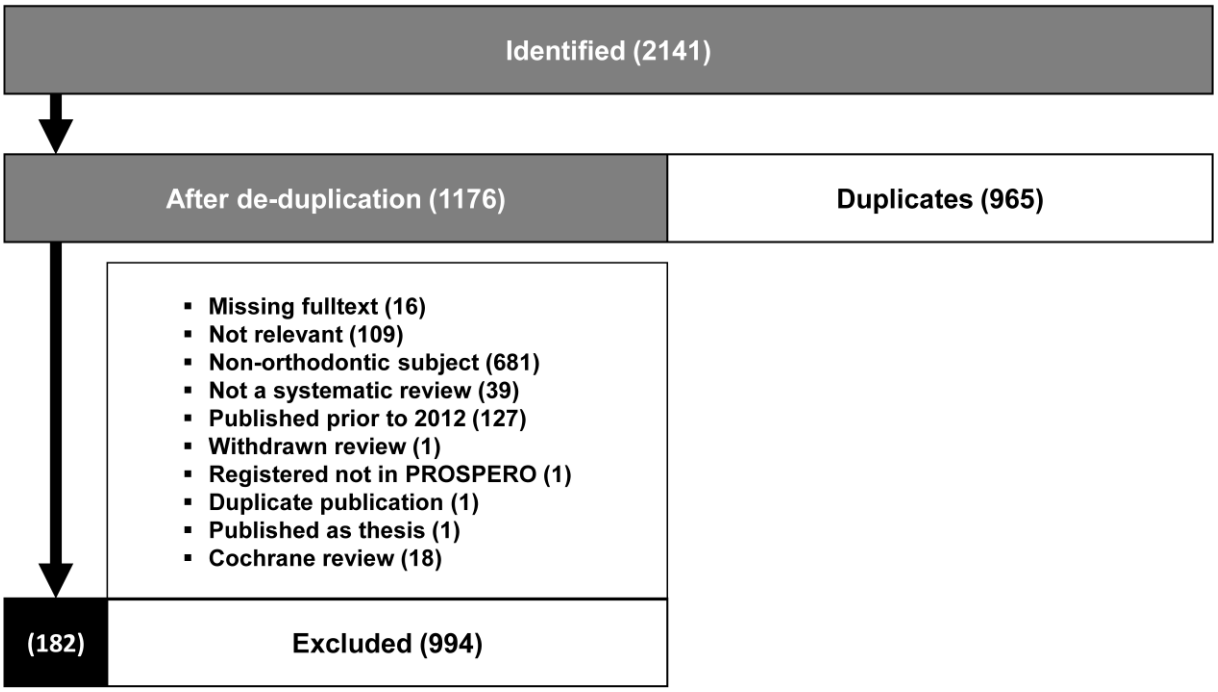
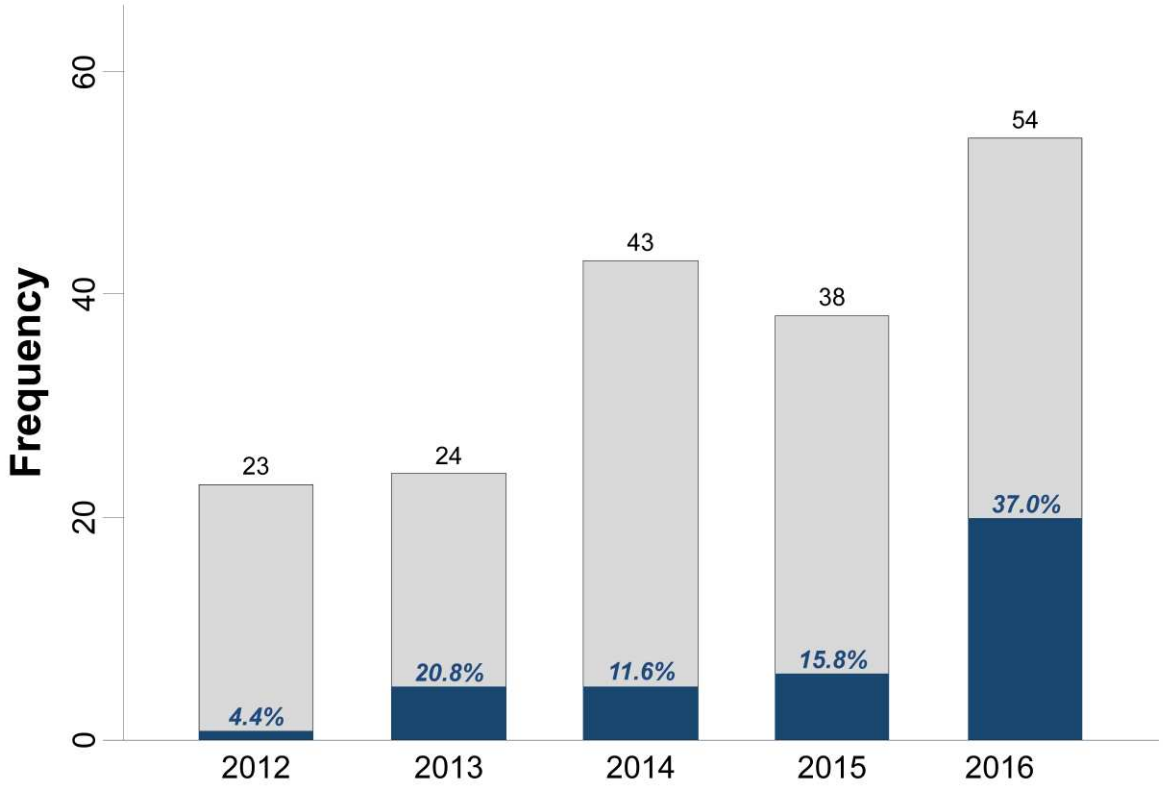


Figure 2. Bar charts indicating the numbers of systematic review included in each year (gray bars) and the percentage of systematic review registered in PROSPERO each year (blue).



Are orthodontic systematic reviews registered *a priori* in PROSPERO?

APPENDICES

Appendix 1. Literature searches performed in all databases with their hits (search date January 10, 2017).

Database	Search strategy	Hits
MEDLINE (via PubMed) www.pubmed.gov	(orthodon* OR orthognath* OR "dentofacial orthopedics" OR "tooth movement" OR "craniofacial growth" OR "growth modification" OR multibracket OR malocclusion OR "fixed appliance" OR cleft* OR "functional appliance") AND ("meta-analysis")	593
Cochrane Database of Systematic Reviews www.cochranelibrary.com	(orthodon* OR orthognath* OR "dentofacial orthopedics" OR "tooth movement" OR "craniofacial growth" OR "growth modification" OR multibracket OR malocclusion OR "fixed appliance" OR cleft* OR "functional appliance")	64
Cochrane Database of Abstracts of Reviews of Effects www.cochranelibrary.com	(orthodon* OR orthognath* OR "dentofacial orthopedics" OR "tooth movement" OR "craniofacial growth" OR "growth modification" OR multibracket OR malocclusion OR "fixed appliance" OR cleft* OR "functional appliance")	149
Embase www.embase.com	orthodon* OR orthognath* OR 'dentofacial orthopedics' OR 'tooth movement'/exp OR 'tooth movement' OR 'craniofacial growth'/exp OR 'craniofacial growth' OR 'growth modification' OR multibracket OR 'malocclusion'/exp OR malocclusion OR 'fixed appliance' OR cleft* OR 'functional appliance' AND ('meta-analysis'/exp OR 'meta-analysis') AND [meta analysis]/lim AND [embase]/lim	415
Scopus www.scopus.com	(orthodon* OR orthognath* OR "dentofacial orthopedics" OR "tooth movement" OR "craniofacial growth" OR "growth modification" OR multibracket OR malocclusion OR "fixed appliance" OR cleft* OR "functional appliance") AND ("meta-analysis")	581
Web of Science www.webofknowledge.com	(orthodon* OR orthognath* OR "dentofacial orthopedics" OR "tooth movement" OR "craniofacial growth" OR "growth modification" OR multibracket OR malocclusion OR "fixed appliance" OR cleft* OR "functional appliance") AND ("meta-analysis")	317
Virtual Health Library www.bvsalud.org/en/	(orthodon* OR orthognath* OR "dentofacial orthopedics" OR "tooth movement" OR "craniofacial growth" OR "growth modification" OR multibracket OR malocclusion OR "fixed appliance" OR cleft* OR "functional appliance") AND ("meta-analysis")	22

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Appendix 2. List of studies excluded/included in this assessment.

No	Paper	Exclusion reason
1	Bergstrand F, Twetman S. Evidence for the efficacy of various methods of treating white-spot lesions after debonding of fixed orthodontic appliances. Journal of clinical orthodontics : JCO. 2003;37(1):19-21.	Mising fulltext
2	Chen Y, Shu WN, He DQ. Effectiveness and safety of power chain versus nickel titanium coil springs in closing dental extraction space: A meta-analysis. Chinese Journal of Evidence-Based Medicine. 2012;12(11):1391-5.	Mising fulltext
3	Dai ML, Xiao M, Yu Z, Liu DX. [Effect of extraction and non-extraction treatment on frontal smiling esthetics: a meta-analysis]. Shanghai kou qiang yi xue = Shanghai journal of stomatology. 2015;24(4):499-504.	Mising fulltext
4	Ge ZL, Jiao X, Tian JH, Yang KH. Clinical effectiveness of vacuum-formed versus Hawley retainers: A systematic review. Chinese Journal of Evidence-Based Medicine. 2012;12(5):596-601.	Mising fulltext
5	Gerke B, Hiersche M, Jones J, Lewis P, Martin M. The effect of the timing of hard palate repair on maxillary growth in the patient with a unilateral cleft lipand palate: A systematic review. Journal of Investigative Medicine. 2014;62(1):168.	Mising fulltext
6	Huo Y, He H, Guo Y, Hua F. Efficacy of low-level diode laser therapy on orthodontic pain management: A systematic review and meta-analysis. Medical Journal of Wuhan University. 2016;37(3):506-11.	Mising fulltext
7	Jiao X, Tian J, Yang K, Ge Z. Clinical effectiveness of vacuum-formed versus Hawley retainers: a systematic review. Chinese Journal of Evidence-Based Medicine. 2012; 12(5):[596-601 pp.].	Mising fulltext
8	Liu ZP, Chen TT, Li GF, Jiang SC, Zou SJ. Meta analysis of soft tissue profile repair in patients treated with and without premolar extraction. Journal of Clinical Rehabilitative Tissue Engineering Research. 2010;14(2):237-9.	Mising fulltext
9	Poletti L, Monti B, Esposito L, Farronato G. Effectiveness of functional appliances in class II malocclusion treatment. Part i. Mondo Ortodontico. 2012;37(5):142-51.	Mising fulltext
10	Poletti L, Tripodi SM, Esposito L, Farronato G. Effectiveness of functional appliances in association with extraoral traction in class II malocclusion treatment. Part II. Mondo Ortodontico. 2012;37(5):152-8.	Mising fulltext
11	Poyak J. Effects of pacifiers on early oral development. International journal of orthodontics (Milwaukee, Wis). 2006;17(4):13-6.	Mising fulltext
12	Sonwane S, Shweta RK, Kumar BS, Shett RGK. Chronic congenital systemic disorder- a hurdle in orthodontic treatment plans: Meta analysis. International Journal of Medical Research & Health Sciences. 2016;5(6):239-47.	Mising fulltext
13	Torlaschi R. Orthodontics and periodontics: A meta-analysis. Giornale dell'Odontoiatra. 2008;25(13):23.	Mising fulltext
14	Wang M, Guo Y, Jiang H. Effectiveness of topical fluoride on prevention of enamel demineralization during the orthodontic treatment in China: A systematic review. Chinese Journal of Evidence-Based Medicine. 2013;13(7):875-84.	Mising fulltext
15	Zhang DP, Liu J, Liu Y, Sun N, Yi JC. [Influence of self-ligating and conventional brackets on dental arch width in non-extraction treatment: a meta analysis]. Shanghai kou qiang yi xue = Shanghai journal of stomatology. 2014;23(3):367-72.	Mising fulltext
16	Zhuge XQ, Zheng Q, Xu X. Meta-analysis of curative effect of distraction osteogenesis surgery on craniofacial deformity secondary to cleft lip and palate. Journal of Clinical Rehabilitative Tissue Engineering Research. 2010;14(7):1162-5.	Mising fulltext
17	Abdallah MN, Flores-Mir C. Are interventions for accelerating orthodontic tooth movement effective? Evidence-based dentistry. 2014;15(4):116-7.	Not relevant to the study
18	Al-Jewair TS, Gaffar BO, Flores-Mir C. Quality assessment of systematic reviews on the efficacy of oral appliance therapy for adult and pediatric sleep-disordered breathing. Journal of Clinical Sleep Medicine. 2016;12(8):1175-83.	Not relevant to the study
19	Allareddy V, Lee MK, Shah A, Elangovan S, Lin CY. Association between study design and citation counts of articles published in the American Journal of Orthodontics and Dentofacial Orthopedics and Angle Orthodontist. Orthodontics : the art and practice of dentofacial enhancement. 2012;13(1):184-91.	Not relevant to the study
20	Al-Riyami S, Moles DR, Cunningham SJ. Orthognathic treatment and temporomandibular disorders: A systematic review. Part 1. A new quality-assessment technique and analysis of study characteristics and classifications. Am J Orthod Dentofacial Orthop 2009;136(5):624.e1-.e15.	Not relevant to the study
21	BeGole EA, Sadowsky C. Methodologies for evaluating long-term stability of dental relationships after orthodontic treatment. Seminars in orthodontics. 1999;5(3):142-50.	Not relevant to the study
22	Birchler FA, Kiliaridis S, Combescure C, Vazquez L. Dental age assessment on panoramic radiographs in a Swiss population: a validation study of two prediction models. Dento maxillo facial radiology. 2016;45(1):20150137.	Not relevant to the study
23	Böhmer AC, Ludwig KU, Knapp M, Steegers-Theunissen RP, Rubini M, Mossey PA, et al. Replication of genome-wide significant susceptibility factors for nonsyndromic cleft lip with or without cleft palate in a European population: Support for 1p36, 1p22.1 and 20q12. Medizinische Genetik. 2013;25(1):142.	Not relevant to the study
24	Böhmer AC, Nagarajan B, Ishorst N, Knapp M, Cotney JL, Nöthen MM, et al. Nonsyndromic cleft lip and palate: Identification of a causal element at 13Q31. Medizinische Genetik. 2016;28(1):100.	Not relevant to the study
25	Bondemark L, Ruf S. Randomized controlled trial: the gold standard or an unobtainable fallacy? Eur J Orthod 2015;37(5):457-61.	Not relevant to the study
26	Bonito AJ, Lux L, Lohr KN. Authors' response [2]. Journal of periodontology. 2006;77(2):323-4.	Not relevant to the study
27	Boonacker CWB, Rovers MM, Browning GG, Hoes AW, Schilder AGM, Burton MJ. Background and introduction. Health Technology Assessment. 2014;18(5):1-+.	Not relevant to the study
28	Bortolus R, Blom F, Filippini F, van Poppel MN, Leoncini E, de Smit DJ, et al. Prevention of congenital malformations and other adverse pregnancy outcomes with 4.0 mg of folic acid: community-based randomized clinical trial in Italy and the Netherlands. BMC pregnancy and childbirth. 2014;14:166.	Not relevant to the study
29	Bykowski MR, Naran S, Winger DF, Losee JE. Abstract 116: the rate of oronasal fistula formation following primary cleft palate surgery: a meta-analysis. Plastic and reconstructive surgery. 2014;133(3 Suppl):132-3.	Not relevant to the study
30	Chia M. Evidence not strong enough to advocate powered toothbrushes over manual for orthodontic patients. Evidence-based dentistry. 2008;9(3):78.	Not relevant to the study
31	Cobourne MT. Finding the evidence is all in the methodology. J Orthod 2014;41(3):165-6.	Not relevant to the study
32	Cunningham Jr LL, Dodson TB, Feinberg SE, Le AD, Wohlford ME, Zuniga JR. 2007 Research Summit: At the Forefront of Innovation. Journal of Oral and Maxillofacial Surgery. 2008;66(2):215-22.	Not relevant to the study
33	Danda AK. Re: Effectiveness of Postoperative Antibiotics in Orthognathic Surgery: A Meta-Analysis, by Danda and Ravi Response. Journal of Oral and Maxillofacial Surgery. 2012;70(9):2024-5.	Not relevant to the study
34	D'Anto V, Bucci R, Franchi L, Rongo R, Michelotti A, Martina R. Class II functional orthopaedic treatment: a systematic review of systematic reviews. Journal of oral rehabilitation. 2015;42(8):624-42.	Not relevant to the study
35	Dawson KH, Chigurupati R. Fixation of mandibular fractures: a tincture of science. Annals of the Royal Australasian College of Dental Surgeons. 2002;16:118-22.	Not relevant to the study
36	De Vries N, Den Herder C, Hessel NS, Hoekema A. Treatment of obstructive sleep apnea syndrome in adults [7] (multiple letters). Nederlands Tijdschrift voor Geneeskunde. 2004;148(5):250-1.	Not relevant to the study
37	Dodson T. Efficacy of biodegradable osteofixation devices in oral and maxillofacial surgery remains inconclusive. Evidence-based dentistry. 2007;8(2):44.	Not relevant to the study
38	Dodson TB. Corticosteroid administration in oral and orthognathic surgery. Evidence-based dentistry. 2011;12(2):49-50.	Not relevant to the study
39	Elkhadem A, Orabi N. Weak evidence suggests higher risk for bracket bonding failure with self-etch primer compared to conventional acid etch over 12 months. Evidence-based dentistry. 2013;14(2):52-3.	Not relevant to the study
40	Elkhadem A. Large overjet may double the risk of dental trauma. Evidence-based dentistry. 2015;16(2):56.	Not relevant to the study
41	Espahbod C, Veitz-Keenan A. Tranexamic acid reduces intraoperative blood loss in orthognathic surgery. Evidence-based dentistry. 2014;15(2):63.	Not relevant to the study
42	Fleming PS, DiBiase AT. Systematic reviews in orthodontics: what have we learned? International dental journal. 2008;58(1):10-4.	Not relevant to the study
43	Fleming PS, Johal A, Pandis N. The effectiveness of laceback ligatures during initial orthodontic alignment: a systematic review and meta-analysis Reply. Eur J Orthod 2013;35(4):548-50.	Not relevant to the study
44	Fleming PS, Koletsi D, Pandis N. Blinded by PRISMA: are systematic reviewers focusing on PRISMA and ignoring other guidelines? PloS one. 2014;9(5):e96407.	Not relevant to the study
45	Fleming PS, Koletsi D, Seehra J, Pandis N. Systematic reviews published in higher impact clinical journals were of higher quality. Journal of clinical epidemiology. 2014;67(7):754-9.	Not relevant to the study
46	Fleming PS, Seehra J, Polychronopoulou A, Fedorowicz Z, Pandis N. Cochrane and non-Cochrane systematic reviews in leading orthodontic journals: a quality paradigm? Eur J Orthod 2013;35(2):244-8.	Not relevant to the study
47	Fleming PS. Accelerating orthodontic tooth movement using surgical and non-surgical approaches. Evidence-based dentistry. 2014;15(4):114-5.	Not relevant to the study
48	Fleming PS. Limited evidence suggests no difference in orthodontic attachment failure rates with the acid-etch technique and self-etch primers. Evidence-based dentistry. 2014;15(2):48-9.	Not relevant to the study
49	Flores-Mir C, Major MP, Major PW. Search and selection methodology of systematic reviews in orthodontics (2000-2004). Am J Orthod Dentofacial Orthop 2006;130(2):214-7.	Not relevant to the study
50	Flores-Mir C. Bonded molar tubes associated with higher failure rate than molar bands. Evidence-based dentistry. 2011;12(3):84.	Not relevant to the study
51	Flores-Mir C. Little evidence to guide initial arch wire choice for fixed appliance therapy. Evidence-based dentistry. 2014;15(4):112-3.	Not relevant to the study
52	Flores-Mir C. No reliable evidence to guide initial arch wire choice for fixed appliance therapy. Evidence-based dentistry. 2013;14(4):114-5.	Not relevant to the study
53	Fox N, Ross Segal G, Schiffman PH, Tuncay OC. Longer orthodontic treatment may result in greater external apical root resorption: What are the treatment-related aetiological factors of external apical root resorption of the maxillary incisor? Evidence-based dentistry. 2005;6(1):21.	Not relevant to the study
54	Fox N. Longer orthodontic treatment may result in greater external apical root resorption. Evidence-based dentistry. 2005;6(1):21.	Not relevant to the study
55	Fricton J. Current evidence providing clarity in management of temporomandibular disorders: summary of a systematic review of randomized clinical trials for intra-oral appliances and occlusal therapies. The journal of evidence-based dental practice. 2006;6(1):48-52.	Not relevant to the study

56	Fricton JR, Ouyang W, Nixdorf DR, Schiffman EL, Velly AM, Look JO. Critical appraisal of methods used in randomized controlled trials of treatments for temporomandibular disorders. Journal of orofacial pain. 2010;24(2):139-51.	Not relevant to the study
57	Gioka C, Eliades T. Materials-induced variation in the torque expression of preadjusted appliances. Am J Orthod Dentofacial Orthop 2004;125(3):323-8.	Not relevant to the study
58	Girardi TLD. Análise cefalométrica de Arnett - revisão de literatura. Ortho Sci, Orthod sci pract. 2011;3(13):488-93.	Not relevant to the study
59	Hani TB, O'Connell AC, Duane B. Casein phosphopeptide-amorphous calcium phosphate products in caries prevention. Evidence-based dentistry. 2016;17(2):46-7.	Not relevant to the study
60	Hanke BA, Motschall E, Turp JC. Association between orthopedic and dental findings: what level of evidence is available? J Orofac Orthop 2007;68(2):91-107.	Not relevant to the study
61	Harman NL, Bruce IA, Kirkham JJ, Tierney S, Callery P, O'Brien K, et al. The Importance of Integration of Stakeholder Views in Core Outcome Set Development: Otitis Media with Effusion in Children with Cleft Palate. PloS one. 2015;10(6):e0129514.	Not relevant to the study
62	He W, Li C, Zou S. Reply to comments on: "Efficacy of low-level laser therapy in the management of orthodontic pain: a systematic review and meta-analysis". Lasers in medical science. 2015;30(2):941-2.	Not relevant to the study
63	How Kau C. Orthodontic retention regimes: will we ever have the answer? Evidence-based dentistry. 2006;7(4):100.	Not relevant to the study
64	Ismail AI, Bader JD. Evidence-based dentistry in clinical practice. Journal of the American Dental Association. 2004;135(1):78-83.	Not relevant to the study
65	Jamilian A, Cannavale R, Piancino MG, Eslami S, Perillo L. Methodological quality and outcome of systematic reviews reporting on orthopaedic treatment for class III malocclusion: Overview of systematic reviews. J Orthod 2016;43(2):102-20.	Not relevant to the study
66	Javidi H, Benson P. The impact of malocclusion and its treatment on the oral health related quality of life of adults, assessed using the Oral Health Impact Profile (OHIP-14). Evidence-based dentistry. 2015;16(2):57-8.	Not relevant to the study
67	Kalha A. Can I intrude? Evidence-based dentistry. 2007;8(1):17.	Not relevant to the study
68	Kalha A. Orthognathic treatment and temporomandibular disorders - part 1. Evidence-based dentistry. 2010;11(3):82-3.	Not relevant to the study
69	Kalha A. Orthognathic treatment and temporomandibular disorders - part 2. Evidence-based dentistry. 2010;11(3):84-5.	Not relevant to the study
70	Kalha AS. Hawley or vacuum-formed retainers following orthodontic treatment? Evidence-based dentistry. 2014;15(4):110-1.	Not relevant to the study
71	Kalha AS. Is anchorage reinforcement with implants effective in orthodontics? Evidence-based dentistry. 2008;9(1):13-4.	Not relevant to the study
72	Kalha AS. Topical fluorides and decalcification around fixed orthodontic appliances: Which topical fluoride preparations are best able to prevent decalcification around fixed orthodontic appliances? Evidence-based dentistry. 2006;7(2):38-9.	Not relevant to the study
73	Kanavakis G, Dombroski MM, Malouf DP, Athanasiou AE. Demographic characteristics of systematic reviews, meta-analyses, and randomized controlled trials in orthodontic journals with impact factor. Eur J Orthod 2016;38(1):57-65.	Not relevant to the study
74	Kau CH. Orthodontic retention regimes: Will we ever have the answer?: How effective are different retention procedures in maintaining tooth position after treatment by orthodontic appliances? Evidence-based dentistry. 2006;7(4):100.	Not relevant to the study
75	Koletsi D, Fleming PS, Eliades T, Pandis N. The evidence from systematic reviews and meta-analyses published in orthodontic literature. Where do we stand? Eur J Orthod 2015;37(6):603-9.	Not relevant to the study
76	Koletsi D, Valla K, Fleming PS, Chaimani A, Pandis N. Assessment of publication bias required improvement in oral health systematic reviews. Journal of clinical epidemiology. 2016;76:118-24.	Not relevant to the study
77	Kuijpers MA, Kuijpers-Jagtman AM. [Orthodontics in general practice 3. Angle Class II/1 malocclusion: one-phase treatment treatment preferred to two-phase treatment]. Nederlands tijdschrift voor tandheelkunde. 2008;115(1):22-8.	Not relevant to the study
78	Long H, Jian F, Lai W. Weak evidence supports the short-term benefits of orthopaedic treatment for Class III malocclusion in children. Evidence-based dentistry. 2014;15(1):21-2.	Not relevant to the study
79	Long H, Lai W. No reliable evidence for the association between dental crowding and caries. Evidence-based dentistry. 2013;14(1):12.	Not relevant to the study
80	Long H, Zhou Y, Lai W. The effectiveness of laceback ligatures during initial orthodontic alignment: a systematic review and meta-analysis. Eur J Orthod 2013;35(4):547-8.	Not relevant to the study
81	Madurantakam P. Fixed or removable function appliances for Class II malocclusions. Evidence-based dentistry. 2016;17(2):52-3.	Not relevant to the study
82	Maia LC, Antonio AG. Systematic reviews in dental research. A guideline. The Journal of clinical pediatric dentistry. 2012;37(2):117-24.	Not relevant to the study
83	Mattos CT, Ruellas AC. Systematic review and meta-analysis: what are the implications in the clinical practice? Dental Press J Orthod 2015;20(1):17-9.	Not relevant to the study
84	McGuinness N. Fixed functional appliances show definite skeletal and dental changes in the short term. Eur J Orthod 2016;38(2):127-8.	Not relevant to the study
85	Meursinge Reynders R, Ladu L, Ronchi L, Di Girolamo N, de Lange J, Roberts N, et al. Insertion torque recordings for the diagnosis of contact between orthodontic mini-implants and dental roots: protocol for a systematic review. Systematic reviews. 2015;4:39.	Not relevant to the study
86	Mossey P. Epidemiology underpinning research in the aetiology of orofacial clefts. Orthodontics & craniofacial research. 2007;10(3):114-20.	Not relevant to the study
87	O'Neill JRS. Functional appliances and mandibular growth — is there an effect?: Do functional appliances enhance mandibular growth in the treatment of skeletal Class II malocclusions? Evidence-based dentistry. 2004;5(3):74.	Not relevant to the study
88	O'Brien K. Longer treatment times with self-ligated orthodontic brackets. Evidence-based dentistry. 2014;15(3):92.	Not relevant to the study
89	O'Neill J. Do lip bumpers work? Evidence-based dentistry. 2009;10(2):48-9.	Not relevant to the study
90	Pandis N, Fleming PS, Worthington H, Dwan K, Salanti G. Discrepancies in Outcome Reporting Exist Between Protocols and Published Oral Health Cochrane Systematic Reviews. PloS one. 2015;10(9):e0137667.	Not relevant to the study
91	Pandis N, Fleming PS, Worthington H, Salanti G. The Quality of the Evidence According to GRADE Is Predominantly Low or Very Low in Oral Health Systematic Reviews. PloS one. 2015;10(7):e0131644.	Not relevant to the study
92	Pandis N. Randomized clinical trials (RCTs) and systematic reviews (SRs) in the context of evidence-based orthodontics (EBO). Seminars in orthodontics. 2013;19(3):142-57.	Not relevant to the study
93	Papadopoulos MA, Gkiaouris I. A critical evaluation of meta-analyses in orthodontics. Am J Orthod Dentofacial Orthop 2007;131(5):589-99.	Not relevant to the study
94	Papadopoulos MA. Meta-analyses and orthodontic evidence-based clinical practice in the 21 century. The open dentistry journal. 2010;4:92-123.	Not relevant to the study
95	Papadopoulos MA. Meta-analysis in evidence-based orthodontics. Orthodontics & craniofacial research. 2003;6(2):112-26.	Not relevant to the study
96	Papageorgiou SN, Antonoglou GN, Tsiranidou E, Jepsen S, Jager A. Bias and small-study effects influence treatment effect estimates: a meta-epidemiological study in oral medicine. Journal of clinical epidemiology. 2014;67(9):984-92.	Not relevant to the study
97	Papageorgiou SN, Dimitraki D, Coolidge T, Kotsanos N. Publication bias & small-study effects in pediatric dentistry meta-analyses. The journal of evidence-based dental practice. 2015;15(1):8-24.	Not relevant to the study
98	Papageorgiou SN, Gölz L, Jäger A, Eliades T, Bourauel C, Afrashtehfar KI. Evidence regarding lingual fixed orthodontic appliances' therapeutic and adverse effects is insufficient. Evidence-based dentistry. 2016;17(2):54-5.	Not relevant to the study
99	Papageorgiou SN, Koretsi V, Jager A. Bias from historical control groups used in orthodontic research: a meta-epidemiological study. Eur J Orthod 2016.	Not relevant to the study
100	Papageorgiou SN, Papadopoulos MA, Athanasiou AE. Assessing small study effects and publication bias in orthodontic meta-analyses: A meta-epidemiological study. Clinical oral investigations. 2014;18(4):1031-44.	Not relevant to the study
101	Papageorgiou SN, Papadopoulos MA, Athanasiou AE. Reporting characteristics of meta-analyses in orthodontics: methodological assessment and statistical recommendations. Eur J Orthod 2014;36(1):74-85.	Not relevant to the study
102	Papageorgiou SN, Tsiranidou E, Antonoglou GN, Deschner J, Jager A. Choice of effect measure for meta-analyses of dichotomous outcomes influenced the identified heterogeneity and direction of small-study effects. Journal of clinical epidemiology. 2015;68(5):534-41.	Not relevant to the study
103	Papageorgiou SN, Xavier GM, Cobourne MT. Basic study design influences the results of orthodontic clinical investigations. Journal of clinical epidemiology. 2015;68(12):1512-22.	Not relevant to the study
104	Papageorgiou SN. Meta-analysis for orthodontists: Part I--How to choose effect measure and statistical model. J Orthod 2014;41(4):317-26.	Not relevant to the study
105	Papageorgiou SN. Meta-analysis for orthodontists: Part II--Is all that glitters gold? Journal of orthodontics. 2014;41(4):327-36.	Not relevant to the study
106	Pickett F. Editor's Consensus Report: Periodontitis and Atherosclerotic Cardiovascular Disease. American Journal of Cardiology. 2010;105(3):424-5.	Not relevant to the study
107	Proffit WR. EVIDENCE AND CLINICAL DECISIONS: Asking the Right Questions to Obtain Clinically Useful Answers. Seminars in orthodontics. 2013;19(3).	Not relevant to the study
108	Rana SS, Kharbanda OP. Letter to editor on "Efficiency of bimaxillary advancement surgery in increasing the volume of the upper airways: a systematic review of observational studies and meta-analysis". Eur Arch Otorhinolaryngol 2016.	Not relevant to the study
109	Reynders RM, de Lange J. Moderate quality evidence that surgical anchorage more effective than conventional anchorage during orthodontic treatment. Evidence-based dentistry. 2014;15(4):108-9.	Not relevant to the study
110	Rinchuse DJ, Rinchuse DJ, Kandasamy S, Ackerman MB. Deconstructing evidence in orthodontics: making sense of systematic reviews, randomized clinical trials, and meta-analyses. World journal of orthodontics. 2008;9(2):167-76.	Not relevant to the study
111	Roberts CT, Semb G, Shaw WC. Strategies for the advancement of surgical methods in cleft lip and palate. Cleft Palate Craniofac J 1991;28(2):141-9.	Not relevant to the study
112	Rosario HD, Oliveira GM, Freires IA, Matos FS, Paranhos LR. Reply to the comment on: "Efficiency of bimaxillary advancement surgery in increasing the volume of the upper airways: a systematic review of observational studies and meta-analysis". Eur Arch Otorhinolaryngol 2016.	Not relevant to the study
113	Ruiz M. Evidence-based orthodontics or the paradigm shift. International orthodontics. 2011;9(1):1-19.	Not relevant to the study
114	Saltaji H, Armijo-Olivo S, Cummings GG, Amin M, Flores-Mir C. Methodological characteristics and treatment effect sizes in oral health randomised controlled trials: Is there a relationship? Protocol for a meta-epidemiological study. BMJ open. 2014;4(2):e004527.	Not relevant to the study
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1080	Long H, Pyakurel U, Wang Y, Liao L, Zhou Y, Lai W. Interventions for accelerating orthodontic tooth movement: a systematic review. Angle Orthodontist. 2013; 83(1):[164-71.	Included
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1082	Long H, Zhou Y, Xue J, Liao L, Ye N, Jian F, et al. The effectiveness of low-level laser therapy in accelerating orthodontic tooth movement: a meta-analysis. Lasers in medical science. 2015;30(3):1161-70.	Included
1083	Machado E, Machado P, Grehs RA, Cunali PA. Orthodontics as a therapeutic option for temporomandibular disorders: A systematic review. Dental Press J Orthod 2012;17(3):98-102.	Included
1084	Machado-Junior AJ, Zancanella E, Crespo AN. Rapid maxillary expansion and obstructive sleep apnea: A review and meta-analysis. Medicina oral, patologia oral y cirugia bucal. 2016;21(4):e465-9.	Included
1085	Mai W, He J, Meng H, Jiang Y, Huang C, Li M, et al. Comparison of vacuum-formed and Hawley retainers: a systematic review. Database of Abstracts of Reviews of Effects. 2014; (2):[720-7.	Included
1086	Major MP, Wong JK, Saltaji H, Major PW, Flores-Mir C. Skeletal anchored maxillary protraction for midface deficiency in children and early adolescents with Class III malocclusion: A systematic review and meta-analysis. Journal of the World Federation of Orthodontists. 2012;1(2):e47-e54.	Included
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1089	Martin-Camean A, Jos A, Camean AM, Solano E, Iglesias-Linares A. Genotoxic and cytotoxic effects and gene expression changes induced by fixed orthodontic appliances in oral mucosa cells of patients: a systematic review. Toxicology mechanisms and methods. 2015;25(6):440-7.	Included
1090	Mattos CT. Análise tomográfica das vias aéreas e sua aplicação em pacientes ortognáticos. 2012:94-.	Included
1091	Meursinge Reynders R, Ronchi L, Ladu L, Van Etten-Jamaludin F, Bipat S. Insertion torque and orthodontic mini-implants: a systematic review of the artificial bone literature. Proceedings of the Institution of Mechanical Engineers Part H, Journal of engineering in medicine. 2013;227(11):1181-202.	Included
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1093	Mickenautsch S, Yengopal V, Banerjee A. Retention of orthodontic brackets bonded with resin-modified GIC versus composite resin adhesives--a quantitative systematic review of clinical trials. Clinical oral investigations. 2012;16(1):1-14.	Included
1094	Migliorati M, Isaia L, Cassaro A, Rivetti A, Silvestrini-Biavati F, Gastaldo L, et al. Efficacy of professional hygiene and prophylaxis on preventing plaque increase in orthodontic patients with multibracket appliances: a systematic review. Database of Abstracts of Reviews of Effects. 2014; (2):[epub p.].	Included
1095	Millett D, Cunningham S, O'Brien K, Benson P, Oliveira C. Treatment and stability of class II division 2 malocclusion in children and adolescents: a systematic review. Am J Orthod Dentofacial Orthop 2012; 142(2):[159-69.	Included
1098	Morales-Fernandez M, Iglesias-Linares A, Yanez-Vico R, Mendoza-Mendoza A, Solano-Reina E. Bone- and dentoalveolar-anchored dentofacial orthopedics for class III malocclusion: new approaches, similar objectives? A systematic review. Angle Orthodontist. 2013; 83(3):[540-52 pp.].	Included
1099	Nascimento L, Souza M, Azevedo A, Maia L. Are self-ligating brackets related to less formation of Streptococcus mutans colonies? A systematic review. Database of Abstracts of Reviews of Effects. 2014; (2):[60-8.	Included
1100	Nascimento PL, Fernandes MT, Figueiredo FE, Faria ESAL. Fluoride-Releasing Materials to Prevent White Spot Lesions around Orthodontic Brackets: A Systematic Review. Brazilian dental journal. 2016;27(1):101-7.	Included
1101	Nazarali N, Altalibi M, Nazarali S, Major MP, Flores-Mir C, Major PW. Mandibular advancement appliances for the treatment of paediatric obstructive sleep apnea: a systematic review. Eur J Orthod 2015;37(6):618-26.	Included
1102	Nucera R, Lo Giudice A, Rustico L, Matarese G, Papadopoulos MA, Cordasco G. Effectiveness of orthodontic treatment with functional appliances on maxillary growth in the short term: A systematic review and meta-analysis. Am J Orthod Dentofacial Orthop 2016;149(5):600-11.e3.	Included
1103	Okada EM, Ribeiro LN, Stuani MB, Borsatto MC, Fidalgo TK, Paula-Silva FW, et al. Effects of chlorhexidine varnish on caries during orthodontic treatment: a systematic review and meta-analysis. Brazilian oral research. 2016;30(1):e115.	Included

1104	Okuno K, Sato K, Arisaka T, Hosohama K, Gotoh M, Taga H, et al. The effect of oral appliances that advanced the mandible forward and limited mouth opening in patients with obstructive sleep apnea: a systematic review and meta-analysis of randomised controlled trials. Journal of oral rehabilitation. 2014;41(7):542-54.	Included
1105	Pacha MM, Fleming PS, Johal A. A comparison of the efficacy of fixed versus removable functional appliances in children with Class II malocclusion: A systematic review. Eur J Orthod 2016;38(6):621-30.	Included
1106	Pacheco-Pereira C, Luca CG, Major P, Flores-Mir C. Variation of orthodontic treatment decision-making based on dental model type: a systematic review. Database of Abstracts of Reviews of Effects. 2014; (2):[epub.	Included
1107	Pandis N, Fleming PS, Spineli LM, Salanti G. Initial orthodontic alignment effectiveness with self-ligating and conventional appliances: a network meta-analysis in practice. Am J Orthod Dentofacial Orthop 2014;145(4 Suppl):S152-63.	Included
1108	Papadopoulos MA, Koumpridou EN, Vakalis ML, Papageorgiou SN. Effectiveness of pre-surgical infant orthopedic treatment for cleft lip and palate patients: a systematic review and meta-analysis. Orthodontics & craniofacial research. 2012;15(4):207-36.	Included
1109	Papageorgiou SN, Golz L, Jager A, Eliades T, Bourauel C. Lingual vs. labial fixed orthodontic appliances: systematic review and meta-analysis of treatment effects. European journal of oral sciences. 2016;124(2):105-18.	Included
1110	Papageorgiou SN, Konstantinidis I, Papadopoulou K, Jager A, Bourauel C. A systematic review and meta-analysis of experimental clinical evidence on initial aligning archwires and archwire sequences. Orthodontics & craniofacial research. 2014;17(4):197-215.	Included
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1112	Papageorgiou SN, Kutschera E, Memmert S, Golz L, Jager A, Bourauel C, et al. Effectiveness of early orthopaedic treatment with headgear: a systematic review and meta-analysis. Eur J Orthod 2016.	Included
1113	Papageorgiou SN, Zogakis IP, Papadopoulos MA. Failure rates and associated risk factors of orthodontic miniscrew implants: a meta-analysis. Am J Orthod Dentofacial Orthop 2012;142(5):577-95.e7.	Included
1114	Parrini S, Rossini G, Castroflorio T, Fortini A, Deregibus A, Debernardi C. Laypeople's perceptions of frontal smile esthetics: A systematic review. Am J Orthod Dentofacial Orthop 2016;150(5):740-50.	Included
1115	Peiro-Guijarro MA, Guijarro-Martinez R, Hernandez-Alfaro F. Surgery first in orthognathic surgery: A systematic review of the literature. Am J Orthod Dentofacial Orthop 2016;149(4):448-62.	Included
1116	Peres KG, Cascaes AM, Nascimento GG, Victora CG. Effect of breastfeeding on malocclusions: a systematic review and meta-analysis. Acta paediatrica (Oslo, Norway : 1992). 2015;104(467):54-61.	Included
1117	Perinetti G, Primozic J, Franchi L, Contardo L. Treatment Effects of Removable Functional Appliances in Pre-Pubertal and Pubertal Class II Patients: A Systematic Review and Meta-Analysis of Controlled Studies. PloS one. 2015;10(10):e0141198.	Included
1118	Perinetti G, Primozic J, Furlani G, Franchi L, Contardo L. Treatment effects of fixed functional appliances alone or in combination with multibracket appliances: A systematic review and meta-analysis. The Angle orthodontist. 2015;85(3):480-92.	Included
1119	Perinetti G, Primozic J, Manfredini D, Lenarda R, Contardo L. The diagnostic potential of static body-sway recording in orthodontics: a systematic review. Database of Abstracts of Reviews of Effects. 2013; (2):[696-705.	Included
1120	Perinetti G, Westphalen GH, Biasotto M, Salgarello S, Contardo L. The diagnostic performance of dental maturity for identification of the circumpubertal growth phases: a meta-analysis. Prog Orthod 2013;14:8.	Included
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1126	Ren C, McGrath C, Yang Y. The effectiveness of low-level diode laser therapy on orthodontic pain management: a systematic review and meta-analysis. Lasers in medical science. 2015;30(7):1881-93.	Included
1127	Rischen RJ, Breuning KH, Bronkhorst EM, Kuijpers-Jagtman AM. Records needed for orthodontic diagnosis and treatment planning: a systematic review. PloS one. 2013;8(11):e74186.	Included
1128	Rodriguez JC, Suarez F, Chan HL, Padial-Molina M, Wang HL. Implants for orthodontic anchorage: success rates and reasons of failures. Implant dentistry. 2014;23(2):155-61.	Included
1129	Rosario HD, Oliveira GM, Freires IA, de Souza Matos F, Paranhos LR. Efficiency of bimaxillary advancement surgery in increasing the volume of the upper airways: a systematic review of observational studies and meta-analysis. Eur Arch Otorhinolaryngol 2016.	Included
1130	Roscoe MG, Meira JB, Cattaneo PM. Association of orthodontic force system and root resorption: A systematic review. Am J Orthod Dentofacial Orthop 2015;147(5):610-26.	Included
1131	Rossini G, Parrini S, Castroflorio T, Deregibus A, Debernardi C. Efficacy of clear aligners in controlling orthodontic tooth movement: a systematic review. Database of Abstracts of Reviews of Effects. 2014; (2):[epub.	Included
1132	Rossini G, Parrini S, Castroflorio T, Deregibus A, Debernardi C. Periodontal health during clear aligners treatment: a systematic review. Database of Abstracts of Reviews of Effects. 2014; (2):[epub.	Included
1133	Saltaji H, Major M, Alfakir H, Al-Saleh M, Flores-Mir C. Maxillary advancement with conventional orthognathic surgery in patients with cleft lip and palate: is it a stable technique?. Journal of Oral and Maxillofacial Surgery. 2012; 70(12):[2859-66 .	Included
1134	Saltaji H, Major M, Altalibi M, Youssef M, Flores-Mir C. Long-term skeletal stability after maxillary advancement with distraction osteogenesis in cleft lip and palate patients: a systematic review. Angle Orthodontist. 2012; 82(6):[1115-22.	Included
1135	Samsonyanová L, Broukal Z. A systematic review of individual motivational factors in orthodontic treatment: Facial attractiveness as the main motivational factor in orthodontic treatment. International Journal of Dentistry. 2014;2014.	Included
1136	San Miguel Moragas J, Oth O, Büttner M, Mommaerts MY. A systematic review on soft-to-hard tissue ratios in orthognathic surgery part II: Chin procedures. Journal of Cranio-Maxillofacial Surgery. 2015;43(8):1530-40.	Included
1137	San MMJ, Cauteren W, Mommaerts M. A systematic review on soft-to-hard tissue ratios in orthognathic surgery part I: maxillary repositioning osteotomy. Database of Abstracts of Reviews of Effects. 2014; (2):[1341-51.	Included
1138	Sandhu SS, Cheema MS, Khehra HS. Comparative effectiveness of pharmacologic and nonpharmacologic interventions for orthodontic pain relief at peak pain intensity: A Bayesian network meta-analysis. Am J Orthod Dentofacial Orthop 2016;150(1):13-32.	Included
1139	Shi Q, Yang S, Jia F, Xu J. Does low level laser therapy relieve the pain caused by the placement of the orthodontic separators?--A meta-analysis. Head & face medicine. 2015;11:28.	Included
1140	Sitzman TJ, Coyne SM, Britto MT. The Burden of Care for Children With Unilateral Cleft Lip: A Systematic Review of Revision Surgery. Cleft Palate Craniofac J 2016;53(4):84-94.	Included
1141	Sousa MVS, Pinzan A, Consolaro A, Henriques JFC, De Freitas MR. Systematic literature review: Influence of low-level laser on orthodontic movement and pain control in humans. Photomedicine and Laser Surgery. 2014;32(11):592-9.	Included
1142	Sundararaj D, Venkatachalapathy S, Tandon A, Pereira A. Critical evaluation of incidence and prevalence of white spot lesions during fixed orthodontic appliance treatment: A meta-analysis. Journal of International Society of Preventive & Community Dentistry. 2015;5(6):433-9.	Included
1143	Sunnak R, Johal A, Fleming PS. Is orthodontics prior to 11 years of age evidence-based? A systematic review and meta-analysis. Journal of dentistry. 2015;43(5):477-86.	Included
1144	Tannure PN, Oliveira CA, Maia LC, Vieira AR, Granjeiro JM, Costa Mde C. Prevalence of dental anomalies in nonsyndromic individuals with cleft lip and palate: a systematic review and meta-analysis. Cleft Palate Craniofac J 2012;49(2):194-200.	Included
1145	Te Veldhuis EC, Te Veldhuis AH, Koudstaal MJ. Treatment management of children with juvenile idiopathic arthritis with temporomandibular joint involvement: A systematic review. Oral surgery, oral medicine, oral pathology and oral radiology. 2014;117(5):581-9.e2.	Included
1146	Tee BC, Sun Z. Mandibular distraction osteogenesis assisted by cell-based tissue engineering: a systematic review. Orthodontics & craniofacial research. 2015;18 Suppl 1:39-49.	Included
1148	Tieu L, Saltaji H, Normando D, Flores-Mir C. Radiologically determined orthodontically induced external apical root resorption in incisors after non-surgical orthodontic treatment of class II division 1 malocclusion: a systematic review. Database of Abstracts of Reviews of Effects. 2014; (2):[48.	Included
1149	Tsichlaki A, Chin SY, Pandis N, Fleming PS. How long does treatment with fixed orthodontic appliances last? A systematic review. Am J Orthod Dentofacial Orthop 2016;149(3):308-18.	Included
1150	Tsichlaki A, O'Brien K. Do orthodontic research outcomes reflect patient values? A systematic review of randomized controlled trials involving children. Database of Abstracts of Reviews of Effects. 2014; (2):[279-85.	Included

1151	Tsui W, Chua H, Cheung L. Bone anchor systems for orthodontic application: a systematic review. International journal of oral and maxillofacial surgery. 2012; 41(11):[1427-38.	Included
1152	Vaid NR, Doshi VM, Vandekar MJ. Class II treatment with functional appliances: A meta-analysis of short-term treatment effects. Seminars in orthodontics. 2014;20(4):324-38.	Included
1153	van der Heijden P, Dijkstra PU, Stellingsma C, van der Laan BF, Korsten-Meijer AG, Goorhuis-Brouwer SM. Limited evidence for the effect of presurgical nasoalveolar molding in unilateral cleft on nasal symmetry: a call for unified research. Plastic and reconstructive surgery. 2013;131(1):62e-71e.	Included
1154	Verweij JP, Houppermans PN, Gooris P, Mensink G, van Merkesteyn JP. Risk factors for common complications associated with bilateral sagittal split osteotomy: A literature review and meta-analysis. J Craniomaxillofac Surg 2016;44(9):1170-80.	Included
1155	Vilani GN, Mattos CT, de Oliveira Ruellas AC, Maia LC. Long-term dental and skeletal changes in patients submitted to surgically assisted rapid maxillary expansion: a meta-analysis. Oral surgery, oral medicine, oral pathology and oral radiology. 2012;114(6):689-97.	Included
1156	Viwattanatipa N, Puntien T, Nanthavanich N. Systematic review and meta-analysis: Mandibular plane change after orthognathic surgery and distraction osteogenesis in cleft lip and palate patients. Orthodontic Waves. 2015;74(2):27-36.	Included
1157	Viwattanatipa N, Puntien T, Thakkinstian A. Systematic review and meta-analysis of maxillary change among 3 surgical techniques in cleft patients. Orthodontic Waves. 2013;72(2):63-76.	Included
1158	von Bremen J, Ruf S. Juvenile idiopathic arthritis-and now?: a systematic literature review of changes in craniofacial morphology. J Orofac Orthop 2012;73(4):265-76.	Included
1160	Yamaguchi K, Lonic D, Lo LJ. Complications following orthognathic surgery for patients with cleft lip/palate: A systematic review. Journal of the Formosan Medical Association. 2016;115(4):269-77.	Included
1161	Yang X, Li C, Bai D, Su N, Chen T, Xu Y, et al. Treatment effectiveness of Frankel function regulator on the Class III malocclusion: a systematic review and meta-analysis. Am J Orthod Dentofacial Orthop 2014;146(2):143-54.	Included
1162	Yang X, Su N, Shi Z, Xiang Z, He Y, Han X, et al. Effects of self-ligating brackets on oral hygiene and discomfort: a systematic review and meta-analysis of randomized controlled clinical trials. International journal of dental hygiene. 2016.	Included
1163	Yang X, Zhu Y, Long H, Zhou Y, Jian F, Ye N, et al. The effectiveness of the Herbst appliance for patients with Class II malocclusion: a meta-analysis. Eur J Orthod 2016;38(3):324-33.	Included
1164	Yepes E, Quintero P, Rueda ZV, Pedroza A. Optimal force for maxillary protraction facemask therapy in the early treatment of class III malocclusion. Eur J Orthod 2014;36(5):586-94.	Included
1165	Yi J, Ge M, Li M, Li C, Li Y, Li X, et al. Comparison of the success rate between self-drilling and self-tapping miniscrews: a systematic review and meta-analysis. Eur J Orthod 2016.	Included
1166	Yi J, Li M, Li Y, Li X, Zhao Z. Root resorption during orthodontic treatment with self-ligating or conventional brackets: a systematic review and meta-analysis. BMC oral health. 2016;16(1):125.	Included
1168	Zawawi KH, Melis M. The role of mandibular third molars on lower anterior teeth crowding and relapse after orthodontic treatment: A systematic review. Scientific World Journal. 2014;2014.	Included
1169	Zhang W, Qu HC, Yu M, Zhang Y. The Effects of Maxillary Protraction with or without Rapid Maxillary Expansion and Age Factors in Treating Class III Malocclusion: A Meta-Analysis. PloS one. 2015;10(6):e0130096.	Included
1170	Zhou Q, Ul Haq AA, Tian L, Chen X, Huang K, Zhou Y. Canine retraction and anchorage loss self-ligating versus conventional brackets: a systematic review and meta-analysis. BMC oral health. 2015;15(1):136.	Included
1171	Zhou Y, Long H, Ye N, Xue J, Yang X, Liao L, et al. The effectiveness of non-surgical maxillary expansion: a meta-analysis. Eur J Orthod 2014;36(2):233-42.	Included
1172	Zhou Y, Wang Y, Wang X, Voliere G, Hu R. The impact of orthodontic treatment on the quality of life a systematic review. BMC oral health. 2014;14:66.	Included
1173	Zhu Y, Li J, Tang Y, Wang X, Xue X, Sun H, et al. Dental arch dimensional changes after adenoidectomy or tonsillectomy in children with airway obstruction: A meta-analysis and systematic review under PRISMA guidelines. Medicine. 2016;95(39):e4976.	Included
1174	Zhu Y, Long H, Jian F, Lin J, Zhu J, Gao M, et al. The effectiveness of oral appliances for obstructive sleep apnea syndrome: A meta-analysis. Journal of dentistry. 2015;43(12):1394-402.	Included
1175	Zurfluh M, Kloukos D, Patcas R, Eliades T. Effect of chin-cup treatment on the temporomandibular joint: a systematic review. Database of Abstracts of Reviews of Effects. 2014; (2):[epub.	Included
1176	Zymperdikas VF, Koretsi V, Papageorgiou SN, Papadopoulos MA. Treatment effects of fixed functional appliances in patients with Class II malocclusion: a systematic review and meta-analysis. Eur J Orthod 2016;38(2):113-26.	Included

Appendix 3. Coding of originating countries of identified reviews by reporting separately only countries with at least 10 systematic reviews.

Country (uncoded)	n	%		Country (coded)	n	%
Australia	4	2.2%		Brazil	27	14.8%
Austria	1	0.6%		Canada	11	6.0%
Belgium	2	1.1%		China	24	13.2%
Brazil	27	14.8%		Greece	10	5.5%
Canada	11	6.0%		Italy	18	9.9%
Chile	1	0.6%		Netherlands	10	5.5%
China	24	13.2%		United Kingdom	12	6.6%
Colombia	1	0.6%		Other	70	38.5%
Czech Republic	1	0.6%				
Denmark	2	1.1%				
France	1	0.6%				
Germany	8	4.4%				
Greece	10	5.5%				
Hong Kong	3	1.7%				
India	4	2.2%				
Iran	2	1.1%				
Iceland	1	0.6%				
Italy	18	9.9%				
Japan	1	0.6%				
Korea	1	0.6%				
Lithuania	1	0.6%				
Netherlands	10	5.5%				
Poland	1	0.6%				
Saudi Arabia	3	1.7%				
South Africa	1	0.6%				
Spain	6	3.3%				
Switzerland	5	2.8%				
Syria	2	1.1%				
Taiwan	3	1.7%				
Thailand	2	1.1%				
USA	8	4.4%				
United Kingdom	12	6.6%				
United Arab Emirates	1	0.6%				
Yemen	4	2.2%				

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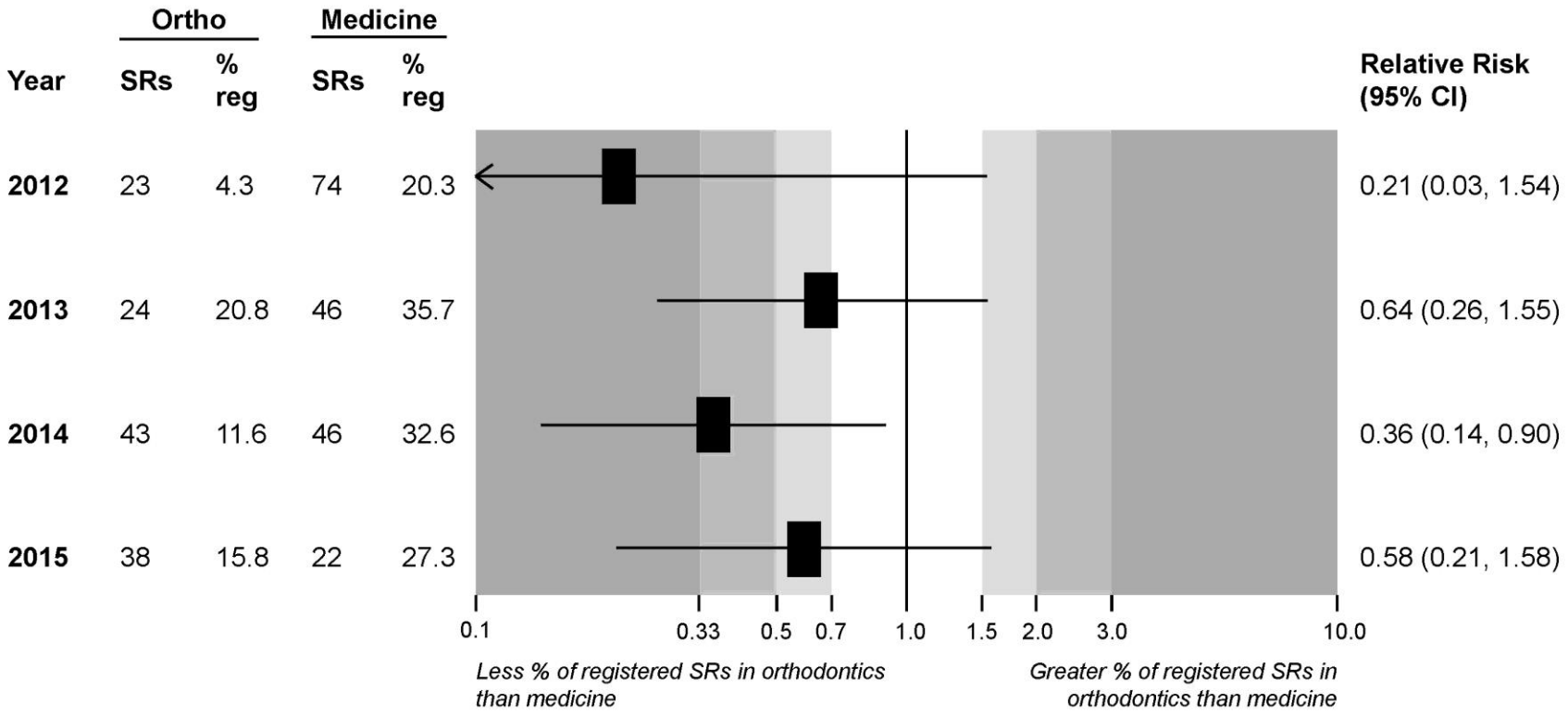
Appendix 4. Comparison of systematic review registration rates between the present study (field of orthodontics) and the results of Tsugimoto et al. (2017) (field of general medicine).



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Appendix 5. Relative contribution of each continent through time in the production of systematic review overall (above) and in the production of systematic review registered in PROSPERO (below).

Systematic reviews produced					
Continent	**Europe**	**N. America**	**S. America**	**Asia**	**Other**
Year	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
2012	11 (47.8%)	5 (21.7%)	4 (17.4%)	2 (8.7%)	1 (4.4%)
2013	11 (45.8%)	2 (8.3%)	3 (12.5%)	7 (29.2%)	1 (4.2%)
2014	24 (55.8%)	3 (7.0%)	8 (18.6%)	8 (18.6%)	0 (0%)
2015	15 (39.5%)	5 (13.2%)	2 (5.3%)	15 (39.5%)	1 (2.6%)
2016	18 (33.3%)	4 (7.4%)	12 (22.2%)	18 (33.3%)	2 (3.7%)
Systematic review registered in PROSPERO					
Continent	**Europe**	**N. America**	**S. America**	**Asia**	**Other**
Year	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
2012	1 (100.0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
2013	3 (60.0%)	0 (0%)	0 (0%)	2 (40.0%)	0 (0%)
2014	2 (40.0%)	0 (0%)	1 (20.0%)	2 (40.0%)	0 (0%)
2015	5 (83.3%)	0 (0%)	1 (16.7%)	0 (0%)	0 (0%)
2016	10 (50.0%)	1 (5.0%)	7 (35.0%)	2 (10.0%)	0 (0%)

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